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Abstracts

Concurrent session 7: Development and tissue engineering

Program/Abstract # 58
Adult stem cells and nanomaterials in skeletal tissue engineering and regeneration

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Understanding nanobiology and application of nanotechnology is important in regenerative medicine, since nanoscale materials are the basic functional subunits of cells and tissues. Stem/progenitor cells are a promising candidate cell type in tissue engineering and regeneration, because of their expandability and multi-differentiation potential. A key requirement in tissue engineering is the three-dimensionality of the regenerate tissue, particularly for weight-bearing musculoskeletal tissues. The challenges in skeletal tissue engineering and regeneration and the application of adult mesenchymal stem cells and nanomaterial scaffolds will be presented. The biology of human mesenchymal stem cells, e.g., proliferation vs differentiation, is intricately regulated by cellcell interactions, signaling by extracellular biofactors, and transcriptional and epigenetic events. Architectural and structure-dependent cues provided by the matrix also guide cell-based tissue morphogenesis. We have developed biomimetic, biodegradable nanofibrous biomaterial scaffolds for cell-based tissue engineering. The fabrication and biological basis of the scale-dependent bioactivities of nanofibrous scaffolds will be presented, as well as their application for cartilage tissue engineering, including articular cartilage, meniscus, and intervertebral disc. The emerging inter-disciplinary research field of tissue engineering is a natural platform for life scientists, engineers, and clinicians working together to advance regenerative medicine.

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Program/Abstract # 59
Tgf-β and intervertebral disc development

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Conditional deletion of Tgf-β type II receptor (Tgfbr2) from type II Collagen expressing cells results in defects in development of the intervertebral disk (IVD). To determine how Tgf-β affects differentiation of mesenchymal progenitor cells, we performed a microarray screen comparing sclerotome cells treated with or without Tgf-β1. A separate microarray screen was done using RNA collected from vertebrae and IVD tissue isolated by laser dissection. From the microarray data, we chose 12 transcription factors that were either regulated by TGF-β or were differentially expressed in the IVD versus the vertebrae for further study. Tgf-β responsiveness of the selected genes was confirmed by semi-quantitative RT-PCR. In situ hybridization analysis was done to determine the expression pattern of selected genes. Interestingly, NFATc1 was specifically localized to the IVD at e12.5. Next, sclerotome cells were encapsulated in a peptide amphiphile matrix with or without integrin RGD binding sites containing MMP degradable sites to determine conditions that permit differentiation of the cells into IVD. The cells were able to survive in the nanomatrix for at least 1week at a density of 10^7cells per ml. When 10ng/ml Tgf-β1 was encapsulated with the cells, scleraxis (*Scx*), a Tgf-β responsive gene, was upregulated indicating that the cells can respond to TGF-β. This model provides an in vitro system to study the role of TGF-β in the development of the IVD. Future experiments will use this model to determine the role of TGF-β regulated transcription factors in IVD development.

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Program/Abstract # 60
A role for Cdc42 in spindle positioning and planar orientation of cell divisions during vertebrate neural tube closure

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Specialization of the cell division process is a common feature of developing embryos, but most studies on vertebrate cell division have focused on cells dividing in culture. Here, we have used *in vivo*-4D confocal microscopy to explore the role of Cdc42 in governing cell division in the developing neural epithelium of *Xenopus laevis*. We find that Cdc42 is critical for stable positioning of the metaphase spindle in these cells, but is not required for spindle positioning in epidermal epithelial cells. We also find that divisions in the *Xenopus* neural plate are planar oriented, and that rotations of mitotic spindles are essential for establishing this orientation. When Cdc42 is disrupted, spindles over-rotate and the final orientation of divisions is changed. Finally, the planar orientation of cell divisions in this tissue appears to be independent of PCP signaling and does not require normal neural morphogenesis. Our data provide new insights